A post-translational modification switch controls coactivator function of histone methyltransferases G9a and GLP.

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Authors: Coralie Poulard, Danielle Bittencourt, Dai-Ying Wu, Yixin Hu, Daniel S Gerke, Michael R Stallcup

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Public Summary:

Scientific Abstract:
Like many transcription regulators, histone methyltransferases G9a and G9a-like protein (GLP) can act gene-specifically as coregulators, but mechanisms controlling this specificity are mostly unknown. We show that adjacent post-translational methylation and phosphorylation regulate binding of G9a and GLP to heterochromatin protein 1 gamma (HP1gamma), formation of a ternary complex with the glucocorticoid receptor (GR) on chromatin, and function of G9a and GLP as coactivators for a subset of GR target genes. HP1gamma is recruited by G9a and GLP to GR binding sites associated with genes that require G9a, GLP, and HP1gamma for glucocorticoid-stimulated transcription. At the physiological level, G9a and GLP coactivator function is required for glucocorticoid activation of genes that repress cell migration in A549 lung cancer cells. Thus, regulated methylation and phosphorylation serve as a switch controlling G9a and GLP coactivator function, suggesting that this mechanism may be a general paradigm for directing specific transcription factor and coregulator actions on different genes.